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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/992,860 | 11/14/2001 | Kuang Yu Chen | RU-0173 | 6007 |

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| EXAMINER | |
|---|---|
| FLOOD, MICHELE C | |
| **ART UNIT** | **PAPER NUMBER** |
| 1655 | |

DATE MAILED: 01/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/992,860 | CHEN ET AL. | |
| | Examiner | Art Unit | |
| | Michele Flood | 1655 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *September 26, 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *38-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/25/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election of the species of orange peel extract in the reply filed on September 26, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

**Claims 38-74 are under examination.**

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an *in vitro* method of inhibiting the growth of cancer cells comprising administering an effective dose amount of a composition comprising a mixture of theaflavin-3-gallate and theaflavin-3'-gallate to cancerous cell lines and/or an *in vivo* method of inhibiting the growth of cancer cells in mice comprising administering to mice an effective dose amount of a composition comprising a mixture of theaflavin-3-gallate and theaflavin-3'-gallate, does not reasonably provide enablement for a method of treating colorectal cancer or a method of treating colorectal cancer in a human, wherein the method suppresses the growth of cancerous colon cells

in the human or a method of treating premalignant colorectal adenoma in a human or a method of treating premalignant colorectal adenoma, wherein the method suppresses the growth of premalignant colorectal adenoma cells in a human or a method of preventing colorectal cancer in a human or a method of preventing colorectal cancer in a human, wherein the method suppresses the growth of colon cells in a human comprising administering to a human an effective amount of theaflavin-3-gallate and theaflavin-3'-gallate to a human in need thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to a method of treating colorectal cancer in a human comprising administering an effective amount of theaflavin-3-gallate and theaflavin-3'-gallate to a human in need thereof; a method of treating colorectal cancer in a human comprising administering to a human in need thereof theaflavin-3-gallate and theaflavin-3'-gallate to a human in an amount to suppress the growth of cancerous colon cells in the human; a method of treating premalignant colorectal adenoma in a human comprising administering an effective amount of theaflavin-3-gallate and theaflavin-3'-gallate to a human in need thereof; a method of treating premalignant colorectal adenoma in a human in need thereof theaflavin-3-gallate and theaflavin-3'-gallate to a human in need thereof in an amount sufficient to suppress the growth of premalignant colorectal adenoma cells in the human; a method of preventing colorectal cancer in a human comprising administering an effective amount of theaflavin-3-gallate and theaflavin-3'-gallate to a human in need thereof; a method of preventing colorectal

cancer in a human comprising administering to a human in need thereof theaflavin-3-gallate and theaflavin-3'-gallate in an amount sufficient to suppress the growth of colon cells in the human.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2D 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

While Applicant has demonstrated an *in vitro* method for the inhibition of the growth for two cancerous cell lines (*i.e.,* virally transformed W138VA cells and Caco-2 human colon cancer cells) comprising the administration of a black tea extract comprising theaflavin-3-gallate and theaflavin-3'-gallate to cancerous cell lines in an amount sufficient to inhibit cancer cell growth, Applicant has not demonstrated a method for treating and/or preventing each of the claim-designated colorectal cancer disease conditions in a human comprising administering an effective amount of theaflavin-3-gallate and theaflavin-3'-gallate to provide any of the functional effects in a human in need thereof, as broadly claimed by Applicant. For instance, on page 11 of the specification, lines 15-33, bridging pages 12-14, Applicant discloses assays for DNA fragmentation analysis, Northern Blot analysis, Reverse transcription polymerase chain

reaction, and Western Blot analysis; however, nowhere in the specification does Applicant show the data from which Applicant has concluded that the claim-designated extract has an effect on modulating Cox-2 gene expression, and nowhere in the specification does Applicant disclose the administration of the claim-designated composition to a human to provide a method of treating and/or preventing any of the claim-designated colorectal disease conditions in a human in need thereof.

It should be noted that the state of the art at the time of filing of the present application suggested that the delivery of therapeutic drugs which exhibit *in vitro* anti-tumor activity do not necessarily have the same beneficial functional effect in humans. For example, Jain (Science, 1996. Vol. 271: 1079-1080) discloses that while promising chemotherapeutic agents exhibit activity against cancer cells *in vitro* and *in vivo* tumor systems, these same agents heralded as breakthrough drugs do not have the same functional effect in humans when delivered to humans bearing tumors. Because of the known unpredictability of the art, in the absence of appropriate experimental evidence, no one skilled in the art would accept the assertion that the claimed administration of the claim-designated ingredients could function as contemplated in the specification, as broadly claimed by Applicant. In another example, Dermer (Bio/Technology, 1994. Vol. 12: 320) states, "The cell lines in which cancer is usually studied are unsuitable for the job. They do not mimic conditions in the human body."

There is no guidance in the specification, other than the aforementioned examples directed to the delivery of an effective amount of black tea extract which comprises a mixture of theaflavin-3-gallate and theaflavin-3'-gallate to *in vitro* cancer

cell cultures for the reduction of cell number and decrease in the level of Cox-2 protein. Hence, given the insufficient guidance in the specification as to how to carry out the instantly claimed invention for the proposed method of therapeutic and/or prophylactic treatment of the claim-designated colorectal disease conditions in a human in need thereof comprising the administration of an effective amount of theaflavin-3-gallate and theaflavin-3'-gallate to a human in need thereof, the lack of working examples, and the lack of correlative working examples, the claims would require an undue amount of experimentation without a predictable degree of success on the part of the skilled artisan to practice the instantly claimed invention, as broadly claimed by Applicant.

According, it would take undue experimentation without a reasonable expectation of success to determine which amounts of the claim-designated composition would have the claimed functional effect for treating and or preventing colorectal cancer or premalignant colorectal adenoma in a human in need thereof comprising administering to the human a composition comprising a mixture of theaflavin-3-gallate and theaflavin-3'-gallate in an amount sufficient to suppress the growth of cancerous colon cells in a human or suppress the growth of premalignant colorectal adenoma cells in a human, and wherein the composition further comprises an orange peel, as broadly claimed, other than the demonstrated *in vitro* and/or *in vivo* method of treating cancer in mice.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele Flood whose telephone number is 571-272-0964. The examiner can normally be reached on 7:00 am - 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michele C. Flood.

MICHELE FLOOD
PRIMARY EXAMINER

Michele Flood
Primary Examiner
Art Unit 1655

MCF
December 12, 2005